REMARKS

Claims 1-13 and 16-20 are pending, with claims 1 and 16 being in independent form. By this Amendment, claims 3, 10-13 and 17-20 have been amended to place the claims in better form for examination.

Applicant maintains that no new matter is presented by this amendment. Accordingly, Applicant respectfully requests that this Amendment be entered.

Objection To The Specification

On Page 3 of the April 21, 2005 Office Action, the specification was objected to as having informalities.

The Examiner stated that the status of applications Serial No. 08/681,219 or 09/230,111 recited at page 17, lines 7-10 have not been provided. The Examiner further stated that there is not Seq. ID. No. for sequence GLGF recited at page 2, line 27 of the instant specification. The Examiner also stated that Applicant is requested to check for other Sequences in the specification that do not have ID. Nos. and to make certain the sequences are in the Sequence Listing and CRF.

By this Amendment, Applicant has amended the specification to indicate the status of applications Serial No. 08/681,219 or 09/230,111 recited at page 17, lines 7-10. The Examiner's attention is directed to the fact that Serial No. 08/681,219 is now U.S. Patent No. 6,911,526, issued June 28, 2005. A Form PTO-1449 which lists U.S. Patent No. 6,911,526 is attached hereto as **Exhibit A**. Applicant requests the Examiner to consider U.S. Patent No. 6,911,526 and then appropriately annotate the Form PTO-1449 with the Examiner's initials to indicate that U.S.

Patent No. 6,911,526 has been considered.

Regarding the Seq. ID. No. for sequence GLGF recited at page 2, line 27 of the instant specification, the Examiner's attention is directed to the Preliminary Amendment filed concurrently with this application on April 8, 2004, by which the specification was amended to include the Seq. ID. No. for sequence GLGF. Another copy of the April 8, 2004 Preliminary Amendment is attached hereto as **Exhibit B**, for the Examiner's reference.

Accordingly, Applicant respectfully requests that the Examiner withdraw the objection to the specification.

Rejection under 35 U.S.C. §112, first paragraph

On page 4 of the April 21, 2005 Office Action, claims 1, 10-13 and 16-20 were rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The Examiner stated that to satisfy a written description requirement for a claimed genus a sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. The Examiner further stated that a representative number of species means that the species which are adequately described are representative of the entire genus. The Examiner also stated that when there is

substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

The Examiner stated that the disclosure of only one species encompassed within a genus adequately describes a claim directed to that genus only if the disclosure indicates that the applicant has invented species sufficient to constitute the genus. The Examiner further stated that the specification provides a written description of proteins in array (beads). The Examiner also stated that it does not provide a description of the claimed generic method wherein the array comprises the other elements such as oligonucleotide, DNA mRNA and sugar.

The Examiner stated that the specification provides only a list of these other elements. The Examiner further stated that a laundry list disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species. The Examiner also stated that it is not readily apparent from the disclosure whether these other elements form a part of the protein, i.e. conjugated or are separate and distinct components of the array.

The Examiner stated that the specification and claim recite for protein-protein interaction between the components in the array (first protein) and the interacting (second) protein. The Examiner further stated that it does not describe the interaction of a protein nucleic acid or protein-sugar. The Examiner also stated that the examples do not provide correlation of the single species to the huge scope of the other elements.

The Examiner stated that neither does it describe the type or

kind, location, length of each of the elements that can be contained in an array or the protein that it interacts with. The Examiner further stated that an applicant of a biotechnological invention cannot necessarily claim a genus after only describing a single species because there may be unpredictability in the results obtained from species other than those specifically described. The Examiner also stated that the disclosure does not describe how each of these components in the array are separated such that the elements do not interact with each other and would only interact with the added protein.

The Examiner stated that Applicant, at the time of filing, is deemed to have not invented species sufficient to constitute the genus by virtue of having disclosed a single species when ... the evidence indicates ordinary artisans could not predict the operability in the invention of any species other than the one disclosed. The Examiner further stated that to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the genus of the invention. The Examiner also stated that as of the filing date, Applicant does not seem to have possession of the claimed method with an array containing the other generic elements.

The Examiner stated that the specification further fails to describe a method wherein the array contains polypeptide rather than protein. The Examiner further stated there is no description in the specification as to the distinguishing characteristics of a protein from a polypeptide or what constitutes a polypeptide, within the claimed method.

By this Amendment, claims 10-13 and 17-20 have been amended to clarify that the oligonucleotide, mRNA, DNA or sugar is complexed

to the first protein or first polypeptide in an array element.

Otherwise, Applicant traverses the rejection.

Claim 1 is directed to a method of preparing a protein array based on biochemical protein-protein interaction, more specifically as between (i) a first protein comprising a PDZ domain, and (ii) a second protein which comprises an amino acid sequence (S/T)-X-(V/I/L)-COOH, with the amino acid sequence (S/T)-X-(V/I/L)-COOH of the second protein binding to the PDZ domain of the first protein. This interaction is central to protein array. However, as demonstrated by the experiments discussed in the application, the proteins may have additional components (for example, oligonucleotide, mRNA, DNA or sugar) complexed to them.

Contrary to the position taken by the Examiner, there is nothing particularly unpredictable about the complexing of the additional components (that is, oligonucleotide, mRNA, DNA or sugar). The protein-protein interaction drives the combination, and the complexing of the additional components is secondary.

Claim 16 is similar to claim 1 except that (a) the first protein is replaced by a first polypeptide comprising a PDZ domain, and (b) the second protein is replaced by a second polypeptide which comprises an amino acid sequence (s/T)-X-(V/I/L)-COOH. However, similar to claim 1, the binding of the amino acid sequence (S/T)-X-(V/I/L)-COOH of the second polypeptide to the PDZ domain of the first polypeptide is central to the interaction.

The term "polypeptide" is well understood in the art to include proteins as well as other molecules including multiple peptides. The discussions of experiments in the application support the

polypeptide-polypeptide interaction (as well as protein-protein interaction). Here, the precise confguration of the polypeptide is not important other than that the first polypeptide comprises a PDZ domain and that the second polypeptide comprises an amino acid sequence (s/T)-X-(V/I/L)-COOH, since these portions of the respective polypeptides are central to the interaction.

Applicant maintains that the application amply provides the required written description of the subject matter claimed.

Accordingly, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C. §112, first paragraph.

Rejection under 35 U.S.C. §112, second paragraph

On page 7 of the April 21, 2005 Office Action, claims 1, 10-13 and 16-20 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

The Examiner stated that claims 10-13 and 17-20 are inconsistent with claims 1 and 16 and it is not clear how a protein-protein interaction, as recited in claims 1 and 16, occur between the structurally different elements of the array e.g., sugar.

By this Amendment, claims 10-13 and 17-20 have been amended to clarify that the oligonucleotide, mRNA, DNA or sugar is complexed to the first protein or first polypeptide in an array element.

The Examiner stated that claim 3 is indefinite and broadens the base claim 1 with the recitation that the "array is used to screen one or more drug targets". The Examiner further stated

that this claim relates to a method of use rather than a method of preparing. The Examiner also stated that the base claim recites only a method of preparing and not a screening method, which would include other steps such that screening would be achieved.

By this Amendment, claim 3 has been amended to clarify the claimed invention of claim 3.

The Examiner stated that claim 16 appears to be a duplicate of claim 1, especially since the specification does not provide a differentiating characteristic between a polypeptide and a protein.

Regarding the difference between claim 1 and claim 16, the term "polypeptide" (as mentioned above) is well understood in the art to include proteins as well as other molecules including multiple peptides. Therefore, claim 16 clearly encompasses additional subject matter not covered by claim 1.

Further, the discussion above in response to the rejection under 35 U.S.C. §112, first paragraph is equally applicable to the rejection under 35 U.S.C. §112, second paragraph, and is incorporated by reference hereby.

Accordingly, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C. §112, second paragraph.

Rejection Under 35 U.S.C. §103(a)

On Page 8 of the April 18, 2005 Office Action, claims 1-9 and 16 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Doyle et al. (1996) "Crystal Structures of a Complexed and

Peptide-Free Membrane Protein-Binding Domain: Molecular Basis of Peptide Recognition by PDZ", Cell, 85:1067-1076, in view of Applicant's disclosure of known prior art, Schneider-Mergener (2001) "Synthetic peptide and protein domain arrays prepared by the SPOT technology", Comp. Funct. Genom., 2:307-309, or Harris et al. (2001) "Mechanism and role of PDZ domains in signaling complex assembly", Jrnl. Cell Science, 114(18):3219-3231.

The Examiner stated that Doyle discloses a modular PDZ domain that binds to the peptide motif T/S-X-Val at the C-terminus of protein K Channels and NMDA receptor ion channels. The Examiner further stated that Doyle discloses that Val can be varied with Ile.

The Examiner acknowlegded, however, that Doyle does not disclose a method of preparing an array for the PDZ domain with its receptor.

The Examiner stated that Applicant discloses at page 3, lines 23-34 that a "recent trend in biology, biotechnology and medicine is the use of arrays of immobilized biological compounds in studies of immunoassays and enzymatic reactions. The Examiner further stated that for example, mass sensing, multianalyte microarray immunoassays have been performed. The Examiner also stated that the use of arrays allows for large scale and high-throughput studies of multiple samples in parallel. The Examiner stated that the integration of microarray technology into the experimental methodology also may increase efficiency in many instances, such as through reducing the volume of samples and reagents required.

The Examiner stated that Harris discloses an array of target proteins to which PDZ containing proteins bind. The Examiner

also stated that Schneider discloses that an array is a versatile toolbox for a variety of applications in proteomics.

The Examiner alleged that it would have been obvious to one ordinary skill in the art at the time the invention was made to prepare or to format the PDZ domains of Doyle into an array since forming a compound into an array will provide a high-throughput screening for a desired receptor or ligand, as taught by Applicant's disclosure and Schneider. The Examiner further alleged that this is evident from the teachings of Harris, which discloses an array of target receptors for the PDZ domain. The Examiner also stated that the numerous advantages cited by Applicant's disclosure and Schneider provides the motivation to one having ordinary skill in the art to make an array for the different PDZ domains.

The Examiner stated that claim 16 is obvious over the teachings of Doyle as to the proteins or polypeptides of PDZ domain at page 1067, column 2.

Applicant maintains that Doyle, Schneider and Harris do not render obvious the invention claimed in claim 1. The claimed invention is patentable over Doyle, Schneider and Harris for at least the following reasons.

The subject application describes high-throughput and low cost methodologies for preparing protein (or polypeptide) arrays based on biochemical interaction between proteins (or polypeptides). More specifically, Applicant found (through experimentation, such as described in the application) that a polypeptide which comprises an amino acid sequence (S/T)-X-(V/I/L)-COOH, is particularly suitable for binding to another polypeptide which comprises a PDZ domain. Moreover, Applicant recognized that the

biochemical interaction between these polypeptides can be harnessed to efficiently prepare polypeptide arrays which keep the polypeptides in a functionally active state and allow, for example, multiple drug screenings under physiological conditions, since the array elements can include oligonucleotides, mRNA, DNA, sugar, etc., complexed to the polypeptide.

Doyle discloses that modular PDZ domains, which are found in many cell junction-associated proteins, mediate the clustering of membrane ion channels by binding to their C-terminus. Through X-ray crystallography, Doyle determined the crystal structures of a complexed and peptide-free membrane protein-binding domain and molecular basis of peptide recognition by PDZ.

As acknowledged by the Examiner, Doyle does not recognize that the interaction between a polypeptide which comprises an amino acid sequence (S/T)-X-(V/I/L)-COOH and another polypeptide which comprises a PDZ domain can be harnessed for preparing polypeptide arrays, such as claimed in independent claims 1 and 16, that would have a plethora of uses.

The Schneider-Mergener paper describes SPOT technology for spatially addressed synthesis of peptide arrays on flat surfaces (such as cellulose, polypropylene or glass). SPOT technology is exemplary of one type of conventional array synthesis technique. The compounds can be coupled by different chemistries through several types of linkers to the flat surfaces, depending on the successive application of the arrays. Attachments via an ester bond or a photocleavable linker allows selective cleavage of the compounds from the surface for the purpose of quality control, or application of the compounds in standard micro-titer plate assay systems.

Applicant does not find teaching or suggestion in the Schneider-Mergener paper that the interaction between a polypeptide which comprises an amino acid sequence (S/T)-X-(V/I/L)-COOH and another polypeptide which comprises a PDZ domain can be harnessed for preparing polypeptide arrays.

Harris is a survey of contemporaneous research involving PDZ domains, including in particular the mechanism and role of PDZ domains in signaling complex assembly.

Applicant does not find teaching or suggestion in Harris that the interaction between a polypeptide which comprises an amino acid sequence (S/T)-X-(V/I/L)-COOH and another polypeptide which comprises a PDZ domain can be harnessed for preparing polypeptide arrays which keep the polypeptides in a functionally active state and allow, for example, multiple drug screenings under physiological conditions.

Applicant does not dispute that array technology has recently been used to facilitate high-throughput experiments.

However, although each of the Doyle paper, the Schneider-Mergener paper and the Harris paper describes bits and pieces of the background art, none of the cited art embodies the recognition that the interaction between a polypeptide which comprises an amino acid sequence (S/T)-X-(V/I/L)-COOH and another polypeptide which comprises a PDZ domain can be harnessed for preparing polypeptide arrays, as provided by independent claims 1 and 14-16.

Accordngly, the cited art does not render the claimed invention obvious.

Regarding claims 2-13, Applicant respectfully points out that claims 2-13 depend on and include all the limitations of claim 1. Thus, claims 2-13 are patentable at least for the reasons set forth above with respect to claim 1.

Regarding claims 17-20, Applicant respectfully points out that claims 17-20 depend on and include all the limitations of claim 16. Thus, claims 17-20 are patentable at least for the reasons set forth above with respect to claim 16.

Accordingly, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C. §103.

Rejection Under 35 U.S.C. §103(a)

On Page 10 of the April 21, 2005 Office Action, claims 1-9 were rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-8 of prior U.S. Patent No. 6,743,630 to Taka-Aki Sato.

The Examiner stated that this is a double patenting rejection. The Examiner further stated that the instant claimed method is coextensive in scope with Sato. The Examiner also stated that the instant application recites a first protein or polypeptide comprising a PDZ domain.

The Examiner stated that the first protein of the instant method is the same as the Sato first proteins since an array cannot contain only one protein. The Examiner further stated that different proteins each comprising a PDZ domain. The Examiner also stated that this claim which recites a first protein in the singular is the same as the method of Sato which recites the first protein in the plural.

Applicant respectfully traverse the rejection.

The rejection is based on the erroneous premise that an array must be based on a plurality of different first proteins or polypeptides, and demonstrates a misunderstanding of the subject matter of this application.

As mentioned above, the binding of the amino acid sequence (S/T)-X-(V/I/L)-COOH of the second protein to the PDZ domain of the first protein array is central to the interaction. However, the first protein itself has the advantage that many components (for example, oligonucleotide, mRNA, DNA, sugar, etc.) can be complexed to it. Similarly, many components can be complexed to the second protein. Thus, contrary to the contention in the Office Action, the array does not need to have a plurality of first proteins.

Applicant respectfully submits that claim 1 of this application covers different subject matter than claims 1-8 of U.S. Patent No. 6,743,630.

Accordingly, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C. §101.

Double Patenting Rejection

On Page 11 of the April 21, 2005 Office Action, claims 1-9 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,743,630 to Sato.

The Examiner stated that although the conflicting claims are not

identical, they are not patentably distinct from each other because the instant claimed method of producing an array containing a single protein is encompassed by Sato which includes said single protein in the plurality of proteins.

Applicant respectfully traverses the rejection.

It is well-established that the claim term "a plurality of" covers two or more but not only one.

Therefore, contrary to the contention in the Office Action, claims 1-8 of U.S. Patent No. 6,743,630 do not encompass claims 1-9 of the present application.

Accordingly, Applicant respectfully requests that the Examiner reconsider and withdraw the rejection of the claims under the judicially created doctrine of obviousness-type double patenting.

In view of the amendments to the claims and remarks hereinabove, Applicants maintain that claims 1-13 and 16-20 are now in condition for allowance. Accordingly, Applicant earnestly solicits the allowance of the application.

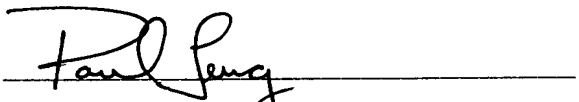
If a telephone interview would be of assistance in advancing prosecution of the subject application, Applicant's undersigned attorneys invite the Examiner to telephone them at the telephone number provided below.

If a petition for an extension of time is required to make this response timely, this paper should be considered to be such a petition.

No fee is deemed necessary in connection with the filing of this

Communication. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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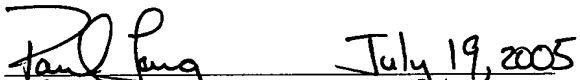
I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.



July 19, 2005
Date

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